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Pregnancy in a patient with hypopituitarism following surgery and radiation for a pituitary adenoma

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ABSTRACT

This is a case of partial hypopituitarism resulting from surgery and radiation for a non-functioning pituitary macroadenoma. The patient had amenorrhea which was secondary to hypogonadotropic hypogonadism and had been on L-thyroxine for central hypothyroidism. For pregnancy, ovulation was induced by gonadotrophins and this was followed by an intrauterine insemination. The antenatal period was uneventful and a Caesarean section was done at 33 weeks when the patient presented with preterm labour. Both infant and mother are well, eight months after delivery.

KEY WORDS: Pregnancy, Hypopituitarism, Radiotherapy, Hypogonadism

Pregnancy is not common in patients with hypopituitarism following surgery and radiation therapy for pituitary macroadenomas. Hormonal dysfunction in these patients involves more than one axis (gonadotrophic, thyroidal and adrenal). Hypogonadotropic hypogonadism can be either of hypothalamic or of pituitary origin, or a combination of both. Pregnancy in this group of patients usually requires the support of assisted reproductive techniques. Ovulation induction is performed with high doses of human menopausal gonadotrophins (HMG). Progesterational support following conception and careful monitoring throughout the antenatal period play a vital role in the successful outcome of pregnancy. We report a subject with such a problem who attended our clinic.

Case History

A 32-year old lady was previously diagnosed to have a non-functioning pituitary macroadenoma at the age of 23 years. She had undergone transfrontal excision of the tumour in 1996 at another centre which was followed by radiotherapy. Thereafter, she developed central hypothyroidism and hypogonadotropic hypogonadism. She was on replacement therapy with L-Thyroxine. Since she desired pregnancy, she attended our clinic. Her clinical examination was unremarkable. Her hormonal profile was as follows : serum Prolactin - 6.27 ng / ml (5 - 25 ng /ml), serum Thyroid Stimulating hormone (TSH) - 0.092 μ IU / ml (0.3 - 4.5 μ IU/ml), serum Luteinizing Hormone (LH) - 0.15 mIU/ml (follicular phase & luteal

phase 0.5 - 18 mIU/ml) , serum Follicle stimulating hormone (FSH) - 0.37 mIU/ml (follicular phase 3.9 -10 ; luteal phase 2.3 - 8 mIU/ml), serum 8 AM Cortisol - 8.57 μ g / dl (7-25 μ g / dl), serum total Thyroxine (T_4) .7.63 μ g/dl (5-12 μ g / dl), serum Free Thyroxine Concentration (FTC)- 0.91 ng/dl (0.8 - 2 ng/dl).

Following assessment in the infertility clinic, she conceived through ovulation induction with Human Menopausal Gonadotrophins (HMG) followed by an intra-uterine insemination with her husband's processed sperms. She had a spontaneous abortion at eight weeks of pregnancy which was the result of not continuing luteal support after conception. Induction with HMG was performed three months later. Ovarian stimulation was commenced with 150 units of HMG, which was increased to 225 units after five days. The total duration of stimulation was 16 days. Human Chorionic Gonadotrophin (HCG) 10,000 IU was administered intramuscularly when the leading follicle crossed 18mm.

After conception, she received progesterational support with micronized vaginal progesterone (Susten). The luteal support with micronised progesterone was continued till 12 weeks of gestation. In the first trimester, the thyroxine dosage was increased to 150 μ g/day and later in the third trimester to 200 μ g/day to maintain a high normal Free Thyroxine concentration (greater than 1.5 ng/dl). The antenatal period was unremarkable. At 33 weeks of gestation, she developed preterm labour. When she was admitted to the clinic, she had a sponta-





neous rupture of membranes. The amniotic fluid was meconium stained. Following a Caesarean section, she delivered a live pre-term female child weighing 2000 gm with an Apgar score of eight. Both infant and mother are well, eight months post-delivery.

Discussion

Pregnancy with underlying hypogonadotrophic hypogonadism is uncommon. Pregnancies have been reported in patients with Sheehan's syndrome.^[2] Kitajima Y *et al* have reported a case that resulted in successful twin pregnancy following panhypopituitarism associated with a suprasellar germinoma.^[1] Our patient had partial hypopituitarism involving the gonadal and thyroid axis following surgery and radiation for a pituitary macroadenoma. Pulsatile gonadotrophin releasing hormone therapy is used mainly in patients with hypogonadotrophic hypogonadism resulting from a hypothalamic cause. In patients with central hypogonadism following hypopituitarism, HMG is used for ovulation induction. It is preferred to recombinant FSH, since it contains both FSH and LH. The latter part of the follicular phase requires LH action in addition to FSH for the final maturation of the follicle.

Higher doses of gonadotrophins and a longer duration of therapy are required for stimulation of follicular growth in these patients since there are no endogenous gonadotrophins. In the case of this patient, it took 16 days to reach an optimum follicle size of 18mm, with a significantly higher gonadotrophin requirement. It has been suggested that the follicular growth and probable pregnancy rate improve when the Growth hormone (GH) and HMG-HCG are combined for ovulation induction in patients with hypogonadotrophic hypogonadism.^[3] It also increases the IGF-1 and IGF-2 activity in the ovary.^[4] However this expensive form of treatment has to be tested in larger studies. LH acts on the corpus luteum to produce progesterone which prepares the endometrium to enter the secretory phase and prepare for implantation of fertilised ovum. In conception cycles, in relation to the process of in vitro fertilization, HCG produced by the embryos continues the stimulatory effects of the corpus luteum and is called the corpus luteum of pregnancy. Since this patient was LH deficient, there was need for exogenous hormone support for the luteal phase.

Once the patient had conceived, she needed luteal support with progesterone for twelve weeks until the placenta produced adequate progesterone in order to avoid early pregnancy loss. The common causes of first trimester pregnancy loss include chromosomal aneuploidies, antiphospholipid antibody syndrome, vaginal infections, uncontrolled sugars and inadequate progesterone support in patients with hypogonadotrophic hypogonadism. The route of replacement of progesterone could be oral, vaginal or intramuscular. Vaginal route application is useful as higher uterine concentrations are obtained when compared to other routes of administration. Intramuscular progesterone use has been shown to give better pregnancy rates though it can cause increased patient discomfort.^[5]

During the antenatal period, constant monitoring of thyroid functions and adjustments of the dosage of thyroxine to keep the free thyroxine concentration in the high normal range is required.^[6] Many patients with hypothyroidism receiving thyroxine therapy require a larger dosage to maintain a euthyroid state when they are pregnant.

Inadequately treated hypothyroidism has been associated with spontaneous miscarriages. A low Intelligent Quotient (IQ) has been found in some of the children of women with suboptimally treated hypothyroxinemia during pregnancy.^[7] This remains to be followed up in this case.

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